Original research article

INTERNATIONAL JOURNAL OF STD & AIDS

International Journal of STD & AIDS
0(0) 1–11

DOI: 10.1177/0956462415578954
std.sagepub.com
SAGE

Loss to follow-up and bias assessment among a cohort of Thai men who have sex with men in Bangkok, Thailand

Sarika Pattanasin[1], Wipas Wimonsate[1], Wannee Chonwattana[1], Jaray Tongtoyai[1], Supaporn Chaikummao[1], Anuwat Sriporn[1], Wichuda Sukwicha[1], Philip A Mock[1] and Timothy H Holtz[1,2]

Abstract

Minimising loss to follow-up is essential to obtain unbiased results. This study aimed to assess factors associated with loss to follow-up and effects on biasing exposure-outcome associations in a cohort of men who have sex with men in Bangkok. We enrolled sexually active Thai men who have sex with men, at least 18 years old, in a study with 4-monthly follow-up visits. At each visit, men answered HIV risk behaviour questions using audio computer-assisted self-interview. Logistic regression was used to evaluate factors associated with loss to follow-up and bias between exposures and prevalent HIV infection were estimated using adjusted relative odds ratios. From 2006 to 2010, we enrolled 1744 men who have sex with men; as of April, 2014, 1256 (72%) had completed at least the month-36 visit; loss to follow-up was 9.6%. Factors independently associated with loss to follow-up were age (18–21 years), education (primary level or less, secondary or vocational education), living outside Bangkok and vicinity, sexual orientation (bisexual, heterosexual), previous HIV testing, HIV infection, and behaviour in the past 4 months (recreational drug use, reporting group sex). An effect of loss to follow-up on factors of prevalent HIV infection was found by sexual orientation (transgender) and unprotected anal intercourse (receptive/insertive). These findings highlight the need to strengthen post-HIV test counselling. Directed counselling for HIV care should be given to young men who have sex with men and recreational drug users.

Keywords

Epidemiology, homosexual, Asia, high-risk behaviour

Date received: 21 October 2014; accepted: 3 March 2015

Introduction

In prospective studies, high loss to follow-up (LTFU) can distort the validity of findings, especially concerning observed behavioural change. Loss to follow-up in cohort studies rarely occurs randomly;[1] differences between study groups of interest can lead to biased findings.[2] Thus, understanding of the characteristics of participants lost to follow-up can improve the quality of cohort studies. Socio-economic factors among study participants have been associated with loss to follow-up among study participants. Several studies related to HIV infection have shown that age,[3,4] literacy,[3] being single,[3] newly diagnosed HIV infection patients,[4] immigrant,[4] geographic distribution,[3] homelessness[3] and injection drug use,[4] were associated with LTFU. In addition, LTFU is less frequent among men who have sex with men (MSM) compared with other high-risk HIV transmission groups.[4] For other health-related studies, achievement of a bachelors degree or higher education,[5] receipt of higher reimbursement for study participation,[5] being retired,[6] and engaging in smoking and binge drinking[6] were

[1]Thailand Ministry of Public Health – US Centers for Disease Control and Prevention Collaboration, Nonthaburi, Thailand
[2]Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, Atlanta, GA, USA

Corresponding author:
Sarika Pattanasin, Thailand MOPH-U.S. CDC Collaboration, Mail: P.O. Box 139, Nonthaburi 11000, Thailand.
Email: vpv6@cdc.gov

associated with LTFU. Demographic factors associated with LTFU have included race and ethnic minority,[5] and low socio-economic status.[5] In contrast, perceived health status has not been associated with LTFU.[5] A better understanding of the prevalence and risk factors associated with LTFU can be beneficial in the management of cohort studies in HIV prevention research.[1,4,7] Knowing the impact of LTFU on estimated associations between exposures and outcomes of interest is essential to understanding the validity of study findings. The purpose of this paper is to determine the prevalence, factors associated with LTFU and effect on biasing exposure-outcome associations in an observational prospective study of MSM in Bangkok, Thailand.

Methods

We recruited participants into the Bangkok MSM Cohort Study (BMCS) at the Silom Community Clinic (SCC) located in central Bangkok. A description of the BMCS has been previously published.[8,9] Eligibility criteria for inclusion in the BMCS included being a Thai national, male at birth, at least 18 years of age, resident of Bangkok or neighboring provinces, reporting penetrative oral or anal sex with another man in the 6 months preceding study entry, committed to at least 36 months of follow-up at 4-month intervals for a maximum of 60 months, and willing and able to provide written informed consent. We conducted enrollment from April 2006 to January 2008 (Period 1) and September 2009 to November 2010 (Period 2).

At enrollment, all MSM were screened for hepatitis B core antibody (Murex Biotec, Dartford, UK or Diasorin, ETI-AB-COREK PLUS kit, Saluggia, Italy), hepatitis B surface antigen (Murex Biotec, Dartford, UK or Serodia, Fujirebio, Tokyo, Japan), hepatitis B surface antibody (Murex Biotec, Dartford, UK or Serodia, Fujirebio, Tokyo, Japan), hepatitis C (Murex Biotec, Dartford, UK), hepatitis A (Murex Biotec, Dartford, UK); urine and rectal swabs (Amplicor STD Swab Specimen Collection and Transport set) were tested for CT (*Chlamydia trachomatis*) and NG (*Neisseria gonorrhea*) by Nucleic Acid Amplification Test (Roche Amplicor®, Roche Diagnostics, Branchburg, NJ, USA); rectal swabs were also cultures for NG. Participants were screened for *Herpes simplex* virus type-1 (HSV-1) and HSV-2 by enzyme-linked immunosorbent assay (HerpeSelect 1 and 2, Focus Diagnostics, Cypress, CA, USA) using venous blood samples. *Treponema pallidum* (TP) screening was performed using the plasma reagin assay (Macro-VueTM RPR 18 mm Circle Card Test, Becton Dickinson Microbiology Systems, Sparks, MD, USA). Specimens with any reactive titer were evaluated with a TP-specific antibody test (DetermineTM Syphilis TP, Abbott Laboratories, Tokyo, Japan) and completed an audio computer-assisted self-interview (ACASI). At each visit, participants were tested for HIV infection using oral fluid and OraQuick® HIV-1/2 Rapid Test (OraSure Technologies Inc., Bethlehem, PA, USA). If reactive, three other HIV rapid tests were performed on blood: (1) Determine™ HIV 1&2, Abbott, Japan; (2) DoubleCheck™ II HIV 1&2 Organics Ltd., Israel, which after February 2011, was replaced with SD-Bioline HIV1 & 2 3.0, Standard Diagnostics, South Korea, and after January 2012 with Double Check Gold™ Ultra HIV 1 & 2, Organics Ltd., Israel; and (3) Cappilus™ HIV-1/HIV-2, Trinity Biotech, USA, which after November 2008 was replaced with Core™ HIV-1/2, UK, and after August 2013 with SD-Bioline HIV1 & 2 3.0. If all three tests were reactive, HIV infection was confirmed, and the result provided to the participant during post-test counselling.

After the enrollment, participants returned for follow-up visits every 4 months to complete an ACASI where they reported their behaviours during the previous 4 months, and underwent HIV testing and counselling. Participants who tested HIV positive were referred for care and treatment if they were eligible for antiretroviral initiation. At each visit, the participants received 500 Thai Baht (about US$16) as compensation for their time and transportation costs. Information concerning the appointment for the next follow-up visit was sent to participants using a short message service (SMS).

For these analyses, time between the enrollment visit and the month-36 follow-up visit served as the observation period. Participants were categorised into three groups i.e. (1) complete follow-up was defined as those who had completed at least 36 months of follow-up by April 1, 2014; (2) incomplete follow-up was defined as those who had missed at least one follow-up visit; (3) LTFU was defined as those who never returned to any follow-up visit.

Statistical analyses

We used counts and proportions to describe socio-demographic characteristics and risk behaviours. Pearson's Chi square and Kruskal-Wallis rank tests were used to test differences between characteristics reported at enrollment and study profiles for categorical and interval variables of interest. A Chi square test was used to assess trends in behaviours by age. Variables associated with LTFU with a $p \leq 0.10$ in bivariate logistic regression were included in multiple logistic regression models. Backward elimination based on likelihood ratio tests was used to determine

variables in the final model (two-sided $p < 0.05$). To determine whether LTFU was associated with differences in exposure-outcome effects, we evaluated factors associated with prevalent HIV infection at enrollment between all participants initially enrolled in the study, and those who were retained to at least one follow-up visit. The primary outcome of the BMCS was to quantify HIV incidence and its predictors; however, HIV status at the follow-up visits among the LTFU were not available; thus, prevalent HIV infection was used as a proxy for incident infection. Unprotected anal intercourse with any partner was categorised based on HIV transmission risk.[10] Following Nohr et al.,[11] we defined adjusted relative odds ratio (adjusted ROR) as the ratio of the adjusted $OR_{\text{retained participant}}$/adjusted $OR_{\text{all participants}}$, and calculated the confidence interval by using the equation method previously described.[11,12] Statistical significance was evaluated using a two-sided $p < 0.05$. We performed all analyses using STATA® (Version 12, 2011; Stata Corp., College Station, Texas, USA).

Ethical review

The Ethical Review Committee for Research in Human Subjects of the Thailand Ministry of Public Health and an Institutional Review Board of the Centers for Disease Control and Prevention (CDC) approved the BMCS protocol.

Results

Participant characteristics at enrollment visit

During Period 1 we enrolled 1292 MSM and during Period 2, we enrolled 452 MSM for a total of 1744 MSM into the study. Of the total, 168 (9.6%) were LTFU, 320 (18.3%) missed at least one follow-up visit, and 1256 (72.0%) completed at least 36 months of follow-up by April 1, 2014. Loss to follow-up was not statistically significantly different by enrollment periods (124/1292 or 9.6% for Period 1; 44/452 or 9.7% for Period 2; $p = 0.93$).

Table 1 presents demographic and behavioural characteristics of participants at enrollment by profile group. The median age of study participants across all three profile groups was 26.0 years (interquartile range [IQR]: 22, 30). Participants LTFU were less likely to live in Bangkok and the surrounding vicinity than those retained in the study. Of 372 participants with prevalent HIV infection, 214 (57.5%) were newly diagnosed i.e. no previous test for HIV infection before enrollment into the BMCS. Study participants LTFU were less likely to have previous HIV testing (30.4%) than those with incomplete (44.4%) and complete (53.8%) profile ($p < 0.001$; Table 1). Among prevalent HIV infection, there was no significant difference between CD4 distribution and study profile ($p = 0.76$; data not shown). Of 57 participants LTFU who were also HIV-infected, 21 (36.8%) had CD4 ≤ 350 cells/mm^3, two (3.5%) had CD4 <50 cells/mm^3, and 46 (80.7%) were newly diagnosed with HIV infection.

Factors associated with LTFU

Table 2 displays the profile of participants LTFU. Multivariate analyses revealed younger age (18–21 years compared with age ≥ 30 years); lower educational level (primary or less and secondary/vocational education versus university or higher education); self-identification as heterosexual/bisexual versus homosexual; living outside Bangkok and the surrounding vicinity; reporting recreational drug use in the past 4 months; not participating in group sex in the past 4 months; never having been HIV-tested; and being HIV-infected were associated with LTFU (Table 2). Of 214 participants newly diagnosed with HIV infection, 46 (21.5%) were LTFU. Compared to participants without HIV or those who were aware of their HIV-infected status, 8.0% (122/1530) were LTFU ($p < 0.01$) (data not shown).

Reporting participation in group sex in the past 4 months increased by age (30.2% among 18–21 years; 35.4% among 22–29 years; 39.4% among ≥ 30 years; p for trend <0.01). In contrast, a Chi square test for trend between recreational drug use in past 4 months and age was not statistically significant (data not shown).

Factors associated with prevalent HIV infection between all participants and those retained (i.e. with at least one follow-up visit)

Of all study participants initially enrolled in the study, 372 (21.3%) had prevalent HIV infection. The estimated adjusted odd ratios of prevalent HIV infection were different for all participants compared to only those retained in some characteristics (transgender, unprotected insertive-only anal intercourse, ever had HIV testing, and recreational drug use in past four months) (Table 3).

Bias assessment

Table 4 shows the adjusted RORs for each of the associated factors of prevalent HIV infection among all and retained participants. Un-identical adjusted ROR (i.e. adjusted ROR and 95% confidence interval was not equal to one) were found by sexual orientation (transgender) and unprotected anal intercourse with any partner (receptive/insertive). Our result demonstrates an

Table 1. Socio-demographic and behaviours at baseline among Thai men who have sex with men (MSM) enrolled in Bangkok MSM Cohort Study 2006–2010, Thailand.

		Study profiles No. (col %)			
	All participants No. (col %)	Loss to follow-up	Incomplete follow-up	Complete follow-up	*p* Value
Period	2006–2010	After enrollment to April 1, 2014			
Total (row %)	1744 (100.0)	168 (9.6)	320 (18.3)	1256 (72.0)	
Age at entry					<0.001
18–21 years old	314 (18.0)	55 (32.7)	71 (22.2)	188 (15.0)	
22–29 years old	935 (53.6)	81 (48.2)	183 (57.2)	671 (53.4)	
≥30 years old	495 (28.4)	32 (19.0)	66 (20.6)	397 (31.6)	
Educational level					<0.001
Primary or less	58 (3.3)	24 (14.3)	7 (2.2)	27 (2.1)	
Secondary/Technical/Vocational	926 (53.1)	115 (68.5)	201 (62.8)	610 (48.6)	
University or higher	760 (43.6)	29 (17.3)	112 (35.0)	619 (49.3)	
Working/studying status					.03
Unemployed	78 (4.5)	8 (4.8)	14 (4.4)	56 (4.5)	
Studying or studying & working	630 (36.1)	63 (37.5)	140 (43.8)	427 (34.0)	
Working only	1036 (59.4)	97 (57.7)	166 (51.9)	773 (61.5)	
Current residence					.01
Bangkok and vicinities[a]	1599 (91.7)	144 (85.7)	295 (92.2)	1160 (92.4)	
Others & no information	145 (8.3)	24 (14.3)	25 (7.8)	96 (7.6)	
Cohabitating with					<0.01
Steady partner	261 (15.0)	17 (10.1)	41 (12.8)	203 (16.2)	
Alone or with roommate	810 (46.4)	96 (57.1)	164 (51.3)	550 (43.8)	
Family	673 (38.6)	55 (32.7)	115 (35.9)	503 (40.0)	
Sexual orientation					<0.001
Bisexual	308 (17.7)	45 (26.8)	52 (16.3)	211 (16.8)	
TG[b]	61 (3.5)	11 (6.5)	17 (5.3)	33 (2.6)	
Homosexual/Gay	1356 (77.4)	103 (61.3)	245 (76.6)	1008 (80.3)	
Heterosexual	19 (1.1)	9 (5.4)	6 (1.9)	4 (0.3)	
Role in anal sex[c]					<0.01
Insertive & Receptive	1088 (63.0)	88 (52.7)	180 (56.8)	820 (65.9)	
Receptive	308 (17.8)	33 (19.8)	70 (22.1)	205 (16.5)	
Insertive	332 (19.2)	46 (27.5)	67 (21.1)	219 (17.6)	
Existing social support[d]					.58
Yes	1507 (86.4)	143 (85.1)	272 (85.0)	1092 (86.9)	

(continued)

Table 1. Continued.

	All participants No. (col %)	Study profiles No. (col %)			*p* Value
		Loss to follow-up	Incomplete follow-up	Complete follow-up	
Comprehensive knowledge on HIV transmission[e]					<0.01
Yes	735 (42.1)	91 (54.2)	134 (41.9)	510 (40.6)	
Ever thought or attempted suicide					.12
Yes	463 (26.5)	55 (32.7)	88 (27.5)	320 (25.5)	
Number of male/TG[b] sexual partners[f] Median (IQR)	4 (2, 10)	5 (2, 11)	4 (2, 9)	4 (2, 10)	.25[h]
Participated in group sex[f]					<0.01
Yes	621 (35.6)	43 (25.6)	106 (33.1)	472 (37.6)	
Binge drinking[f,g]					<0.001
Yes	208 (11.9)	34 (20.2)	51 (15.9)	123 (9.8)	
Erectile dysfunction drug use[f]					.48
Yes	202 (11.6)	24 (14.3)	38 (11.9)	140 (11.1)	
Ever had HIV test					<0.001
Yes	869 (49.8)	51 (30.4)	142 (44.4)	676 (53.8)	
HIV status					<0.001
Positive[h]	372 (21.3)	57 (33.9)	64 (20.0)	251 (20.0)	

[a]Patumthani, Nonthaburi, Samutprakarn and Nakorn Phathom.
[b]TG: transgender person.
[c]Number may not total to 1744 because of missing data.
[d]An existence of someone in family or friend to talk to.
[e]The correct answer to all four questions i.e. condom can protect HIV transmission during vaginal sex, condom can protect HIV transmission during anal sex, HIV can be transmitted through sharing needles and syringes, and a person living with HIV can look healthy.
[f]Timeframe is past four months.
[g]Alcohol intoxication two or three times per week.
[h]Kruskal-Wallis equality-of-populations rank test.
[i]Median CD4 count 413 (IQR 306, 545) cells/mm^3 and median plasma viral load 37,500 (IQR 10,030, 128,000) copies/mL.

Table 2. Socio-demographic and behavioural factors associated with loss to follow-up and attrition of Thai men who have sex with men (MSM) enrolled in Bangkok MSM Cohort Study, Thailand 2006–2010.

	Loss to follow-up					
	Yes		No		Multivariate	
Baseline characteristics	n	%	N	%	AOR	95% CI
Total	168	9.6	1576	90.4		
Age						
18–21 years old	55	17.5	259	82.5	2.1	1.3–3.6
22–29 years old	81	8.7	854	91.3	1.4	0.9–2.2
≥30 years old	32	6.5	463	93.5	1	
Educational level						
Primary or less	24	41.4	34	58.6	8.4	4.2–16.9
Secondary/Technical/Vocational	115	12.4	811	87.6	2.0	1.2–3.1
University or higher	29	3.8	731	96.2	1	
Current province address						
Others & no information	24	16.6	121	83.4	1.7	1.04–2.9
Bangkok and vicinities[a]	144	9.0	1455	91.0	1	
Sexual orientation						
Transgender	11	18.0	50	82.0	1.6	0.8–3.4
Bisexual	45	14.6	263	85.4	1.9	1.3–2.8
Heterosexual	9	47.4	10	52.6	7.4	2.6–20.9
Homosexual	103	7.6	1253	92.4	1	
Participated in group sex[b]						
Yes	43	6.9	578	93.1	0.6	0.4–0.8
No	125	11.1	998	88.9	1	
Recreational drug use[b]						
Yes	51	17.1	248	82.9	1.9	1.3–2.8
No	117	8.1	1328	91.9	1	
Ever had HIV test						
Yes	51	5.9	818	94.1	0.6	0.4–0.9
No	117	13.4	758	86.6	1	
HIV status						
Positive	57	15.3	315	84.7	2.2	1.5–3.2
Negative	111	8.1	1261	91.9	1	
Binge drinking[b,c]					NS	
Yes	34	16.3	174	83.7		
No	134	8.7	1402	91.3		
Role in anal sex					NS	
Insertive & Receptive	88	8.1	1000	91.9		
Receptive	33	10.7	275	89.3		
Insertive	46	13.9	286	86.1		

NS: Not remained in the final multivariate model based on Likelihood ratio test ($p \geq 0.05$).

Variables not shown in the table were not included in multivariate model (working/studying status, cohabitating with, multiple partners, ED [erectile dysfunction] drug use, existing of social support, ever thought or attempted suicide, comprehensive knowledge on HIV transmission[d]).

[a]Patumthani, Nonthaburi, Samutprakarn and Nakorn Phathom.

[b]Timeframe is past 4 months.

[c]Alcohol intoxication two or three times per week.

Table 3. Comparison of factors associated with prevalent HIV infection among all participants and retained participants among Thai men who have sex with men (MSM) enrolled in Bangkok MSM Cohort Study, Thailand 2006–2010.

	Prevalent HIV infection												
	All participants (n = 1744)							Retained participants (n = 1576)					
	Yes		No		Multivariate[a]			Yes		No		Multivariate[b]		
Baseline characteristics	n	%	N	%	AOR	95% CI	p	n	%	N	%	AOR	95% CI	p
Total	372	21.3	1372	78.7				315	20.0	1261	80.0			
Age														
18–21 years old	50	15.9	264	84.1	0.4	0.2–0.6	<.01	39	15.1	220	84.9	0.4	0.3–0.6	<.01
22–29 years old	211	22.6	724	77.4	0.8	0.6–1.1	.19	182	21.3	672	78.7	0.9	0.7–1.2	.50
≥30 years old	111	22.4	384	77.6	1			94	20.3	369	79.7	1		
Educational level														
Primary or less	1	36.2	37	63.8	3.8	2.0–6.9	<.01	15	44.1	19	55.9	5.9	2.8–12.3	<.01
Secondary/Technical/Vocational	227	24.5	699	75.5	2.0	1.6–2.7	<.01	190	23.4	621	76.6	2.3	1.7–3.0	<.01
University or higher	124	16.3	636	83.7	1			110	15.0	621	85.0	1		
Current province address					NS							Not included[c]		
Others & no information	39	26.9	106	73.1				27	22.3	94	77.7			
Bangkok and vicinities[d]	333	20.8	1266	79.2				288	19.8	1167	80.2			
Sexual orientation														
Transgender	8	13.1	53	86.9	0.4	0.2–0.8	.01	8	16.0	42	84.0	0.7	0.3–1.5	.32
Bisexual	53	17.2	255	82.8	0.7	0.5–0.9	.02	40	15.2	223	84.8	0.7	0.5–1.0	.05
Heterosexual	0	0.0	19	100.0	N/A	N/A		0	0.0	10	100.0	N/A	N/A	
Homosexual	311	22.9	1045	77.1	1			267	21.3	986	78.7	1		
Participated in group sex[e]														
Yes	160	25.8	461	74.2	1.5	1.1–1.9	<.01	145	25.1	433	74.9	1.6	1.2–2.1	<.01
No	212	18.9	911	81.1	1			170	17.0	828	83.0	1		
Unprotected anal intercourse with any partner[e]														
Yes, receptive/insertive	201	25.2	597	74.8	1.4	1.1–1.8	.01	172	23.6	557	76.4	1.3	1.0–1.7	.04
Yes, insertive only	22	13.2	144	86.8	0.6	0.4–1.1	.09	16	10.5	136	89.5	0.5	0.3–0.9	.03
No	149	19.1	631	80.9	1			127	18.3	568	81.7	1		
Ever had HIV test												NS		
Yes	158	18.2	711	81.8	0.7	0.5–0.8	<.01	147	18.0	671	82.0			
No	214	24.5	661	75.5	1			168	22.2	590	77.8			

(continued)

Table 3. Continued.

	Prevalent HIV infection													
	All participants (n = 1744)							Retained participants (n = 1576)						
	Yes		No		Multivariate[a]			Yes		No		Multivariate[b]		
Baseline characteristics	n	%	N	%	AOR	95% CI	p	n	%	N	%	AOR	95% CI	p
Recreational drug use[e]											NS			
Yes	84	28.1	215	71.9	1.4	1.1–1.9	.02	66	26.6	182	73.4			
No	288	19.9	1157	80.1	1			249	18.7	1079	81.3			
Binge drinking[e,f]					Not included[c]							NS		
Yes	53	25.5	155	74.5				43	24.7	131	75.3			
No	319	20.8	1217	79.2	1			272	19.4	1130	80.6			
Erectile dysfunction drug use[e]					NS							Not included[c]		
Yes	55	27.2	147	72.8				43	24.2	135	75.8			
No	317	20.6	1225	79.4				272	19.5	1126	80.5			

CI: confidence interval.

NS: Not remained in the final multivariate model based on Likelihood ratio test ($p \geq 0.05$). Among all participants; current province address ($p = .22$), erectile dysfunction drug use ($p = .46$). Among retained participants; ever had HIV test ($p = .06$), recreational drug use ($p = .08$) and binge drinking ($p = .53$).

Variables not show in the table were not included in multivariate model (existing of social support, ever thought or attempted suicide and comprehensive knowledge on HIV transmission [correctly answer to all four questions i.e. condom can protect HIV transmission during vaginal sex, condom can protect HIV transmission during anal sex, HIV can be transmitted through sharing needles and syringes, and a person living with HIV can look healthy]).

[a]1725 observations included in the final model.

[b]1566 observations included in the final model.

[c]Not included: Not include in the multivariate model ($p > 0.10$).

[d]Patumthani, Nonthaburi, Samutprakarn, and Nakorn Phathom.

[e]Timeframe is past 4 months.

[f]Alcohol intoxication two or three times per week.

Table 4. Adjusted relative ORs (ROR) of factors associated with prevalent HIV infection among all participants and retained participants among Thai men who have sex with men (MSM) enrolled in Bangkok MSM Cohort Study, Thailand 2006–2010.

	Prevalent HIV infection					
	All participants (n = 1744)		Retained participants (n = 1576)			
Associated factors	AOR	95% CI	AOR	95% CI	Adjusted ROR	95% CI[a]
Age						
18–21 years old	0.4	0.2–0.6	0.4	0.3–0.6	1.0	0.9–1.1
22–29 years old	0.8	0.6–1.1	0.9	0.7–1.2	1.1	1.0–1.3
≥30 years old	1		1		1	
Educational level						
Primary or less	3.8	2.0–6.9	5.9	2.8–12.3	1.6	0.03–76.7
Secondary/Technical/Vocational	2.0	1.6–2.7	2.3	1.7–3.0	1.1	0.8–1.6
University or higher	1		1		1	
Sexual orientation						
Transgender	0.4	0.2–0.8	0.7	0.3–1.5	1.7	1.1–2.6
Bisexual	0.7	0.5–0.9	0.7	0.5–1.0	1.0	0.9–1.1
Heterosexual	N/A	N/A	N/A	N/A	N/A	N/A
Homosexual	1		1		1	
Participated in group sex[b]						
Yes	1.5	1.1–1.9	1.6	1.2–2.1	1.1	0.9–1.4
No	1		1		1	
Unprotected anal intercourse with any partner[b]						
Yes, receptive/insertive	1.4	1.1–1.8	1.3	1.0–1.7	0.9	0.86–0.94
Yes, insertive only	0.6	0.4–1.1	0.5	0.3–0.9	0.8	NA
No	1		1		1	

AOR: adjusted odd ratio; ROR: relative adjusted odd ratio; CI: confidence Interval: NA: Interval cannot estimated due to $SE_{retained} < SE_{all}$.
[a]The interval estimated ROR*exp (±1.96*se).
[b]Timeframe is past 4 months.

effect of LTFU on factors of prevalent HIV infection. LTFU resulted in an overestimate of association between prevalent HIV infection and sexual orientation (transgender) but an underestimate of association between prevalent HIV infection and unprotected anal intercourse with any partner (receptive/insertive).

Discussion

Our results demonstrate that only 10% of high-risk Thai MSM enrolled in the BMCS were LTFU by month-36. Young age (18–21 years), less than secondary education, use of recreational drugs in past 4 months, no previous HIV testing, being HIV-infected, reporting being heterosexual/bisexual, living outside Bangkok and the surrounding vicinity were associated with LTFU. These are characteristics similar to the profile of high-risk sexually active young Thai MSM disproportionately affected by HIV infection.[13,14] Finally, based on the bias estimate (adjusted ROR) LTFU biased the association between risk characteristics (i.e. sexual orientation: transgender; unprotected anal intercourse: receptive/insertive) and prevalent HIV infection.

We found that characteristics of participants LTFU were similar to those previously reported.[3–6] Our results raise an important issue concerning HIV risk behaviour, young MSM were less likely to return for the follow-up visit, which could result in an underestimate of risk behaviour associations in longitudinal studies, given the available data that suggests that they are a high HIV-incidence group.[8,15] Recreational drug users and HIV-infected MSM are less likely to return for follow-up visits, especially when newly diagnosed with HIV infection, consistent with previous reports that people who inject drugs or who are newly diagnosed with HIV are at risk for being LTFU.[4] Our participants may have been unaware of their HIV status before being enrolled into the BMCS; only half had ever had an HIV test prior to enrollment in the study. Recently diagnosed participants may not have fully addressed their health needs, been in denial, or had not yet created a strong link with a care provider or facility.[4] Effective voluntary counselling and testing services emphasising

post-HIV counselling is needed to provide a more intensive support for individuals with newly diagnosed HIV infection.

Recreational drug use in past 4 months has been associated with high-risk behaviours in other studies among MSM,[16–20] suggesting the MSM population is at high risk for HIV infection. LTFU among recreational drug users can introduce bias in estimating associations between HIV infection and other factors. Our analyses failed to detect a relationship between sexual orientation (i.e. transgender), ever having had an HIV test, and recreational drug use in past 4 months with prevalent HIV infection when data for one-sixth (17%) of the original study sample was excluded due to LTFU.

Participation in group sex in past 4 months was negatively associated with LTFU, an unexpected finding given sex party participation and use of recreational drugs ('high party sex') has been reported in many MSM studies.[20,21] Younger participants were less likely to engage in group sex than older participants; however, the distribution of recreational drug use in past 4 months was similar between age groups. The association between young age and LTFU may explain the effect of participation in group sex in past 4 months and LTFU in our results.

The present study examined the effect of LTFU on the associated factors of prevalent HIV infection. We found that the adjusted relative ORs between the retained and all participants were nearly identical to most associated factors, except unprotected anal intercourse with any partner (receptive/insertive) and sexual orientation (transgender), especially as the bias estimate (adjusted ROR) of sexual orientation (transgender) exceeded 70%. Our findings demonstrate that LTFU significantly biased the association between prevalent HIV infection and sexual orientation (transgender) as well as prevalent HIV infection and unprotected anal intercourse with any partner (receptive/insertive). Although our LTFU proportion was similar to other HIV prospective studies,[4,7] we cannot rule out that non-probability sampling (i.e. convenience sampling), which was used to approach the study participants, may have introduced some bias. However, to apply probability sampling to a subpopulation such as MSM is impossible, given that no sampling frame is available for this population. Our results show an example of how LTFU can distort the validity of findings in a study on prevalent HIV infection among a MSM cohort. We recommend bias estimation should be a part of all cohort studies conducted to investigate HIV infection among subpopulations. We identified 15% of LTFU among HIV-infected MSM, similar to 12% LTFU previously reported among HIV-infected Thai adults starting highly active antiretroviral therapy (HAART)[7] and 17% among newly HIV-diagnosed persons in a French database.[4] In addition, a low CD4 count (<50 cells/mm^3) was associated with LTFU among HIV-infected after initiation of antiretroviral therapy.[3] In our cohort, more than one-third (37%) of those LTFU who were also HIV-infected were eligible for ART according to the Thailand national guidelines for antiretroviral therapy at the time of analyses (i.e., start ART at CD4 <350 cells/mm^3 [22]). We were not able to determine outcomes (e.g. clinical progression and viral load) for HIV-infected persons who were LTFU in this study.

This study included several limitations. MSM enrolled in the BMCS may not have been representative of the Bangkok MSM community at large because participants were not randomly selected. In addition, desirability bias may have caused under-reporting of sexual and drug use risk behaviours. Lastly, information on specific variables related to LTFU e.g. subject reimbursement for interview, migrant, and retirement were not collected.

Our study demonstrates that future longitudinal cohort studies conducted among MSM in Bangkok should integrate specific measures to minimise LTFU. Special attention should be given to young MSM and those with lower levels of education. Post-HIV test counseling and directed counselling for participants who use recreational drugs are needed to ensure the retention of high-risk participants, not only to ensure validity of study findings but also to provide treatment and care to these vulnerable MSM.

Acknowledgments

We acknowledge the participants of the Bangkok Men Who Have Sex With Men Cohort Study for their time and efforts. In addition, this research could not be possible without the dedication and expertise of the staff at the Silom Community Clinic.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The US Centers for Disease Control and Prevention sponsored this study.

References

1. Kristman V, Manno M and Cote P. Loss to follow-up in cohort studies: how much is too much? *Eur J Epidemiol* 2004; 19: 751–760.

2. Dettori JR. Loss to follow-up. *Evid Based Spine Care J* 2011; 2: 7–10.
3. Alvarez-Uria G, Naik PK, Midde M, et al. Predictors of loss to follow-up after engagement in care of HIV-infected children ineligible for antiretroviral therapy in an HIV cohort study in India. *Germs* 2014; 4: 9–15.
4. Lanoy E, Mary-Krause M, Tattevin P, et al. Predictors identified for losses to follow-up among HIV-seropositive patients. *J Clin Epidemiol* 2006; 59: 829–835.
5. DeVita DA, White MC, Zhao X, et al. Determinants of subject visit participation in a prospective cohort study of HTLV infection. *J Clin Epidemiol* 2006; 59: 829–835.
6. Goldberg M, Chastang JF, Zins M, et al. Health problems were the strongest predictors of attrition during follow-up of the GAZEL cohort. *J Clin Epidemiol* 2006; 59: 1213–1221.
7. Fregonese F, Collins IJ, Jourdain G, et al. Predictors of 5-year mortality in HIV-infected adults starting highly active antiretroviral therapy in Thailand. *J Acquir Immune Defic Syndr* 2012; 60: 91–98.
8. van Griensven F, Thienkrua W, McNicholl J, et al. Evidence of an explosive epidemic of HIV infection in a cohort of men who have sex with men in Thailand. *AIDS* 2013; 27: 825–32.
9. Holtz TH, Thienkrua W, McNicholl JM, et al. Prevalence of *Treponema pallidum* seropositivity and herpes simplex virus type 2 infection in a cohort of men who have sex with men, Bangkok, Thailand, 2006–2010. *Int J STD & AIDS* 2012; 23: 424–428.
10. Patel P, Borkowf CB, Brooks JT, et al. Estimating per-act HIV transmission risk: a systematic review. *AIDS* 2014; 28: 1509–1519.
11. Nohr EA, Frydenberg M, Henriksen TB, et al. Does low participation in cohort studies induce bias? *Epidemiology. 2006* 17: 413–418.
12. Osler M, Kriegbaum M, Christensen U, et al. Loss to follow up did not bias associations between early life factors and adult depression. *J Clin Epidemiol* 2008; 61: 958–963.
13. Koblin BA, Torian LV, Guilin V, et al. High prevalence of HIV infection among young men who have sex with men in New York City. *AIDS* 2000; 14: 1793–1800.
14. Balaji AB, Bowles KE, Le BC, et al. High HIV incidence and prevalence and associated factors among young MSM, 2008. *AIDS* 2013; 27: 269–278.
15. Beyrer C, Baral SD, Griensven FV, et al. HIV in men who have sex with men 1 Global epidemiology of HIV infection in men who have sex with men. *Lancet* 2012; 380: 367–377.
16. Stall R, McKusick L, Wiley J, et al. Alcohol and drug use during sexual activity and compliance with safe sex guidelines for AIDS: the AIDS Behavioral Research Project. *Health Educ Quart* 1986; 13: 359–371.
17. Mansergh G, Colfax GN, Marks G, et al. The Circuit Party Men's Health Survey: findings and implications for gay and bisexual men. *Am J Public Health* 2001; 91: 953–958.
18. Mansergh G, Shouse RL, Marks G, et al. Methamphetamine and sildenafil (Viagra) use are linked to unprotected receptive and insertive anal sex, respectively, in a sample of men who have sex with men. *Sex Transm Infect* 2006; 82: 131–134.
19. Vaudrey J, Raymond HF, Chen S, et al. Indicators of use of methamphetamine and other substances among men who have sex with men, San Francisco, 2003–2006. *Drug Alcohol Depen* 2007; 90: 97–100.
20. Pantalone DW, Bimbi DS and Parsons JT. Motivations for the recreational use of erectile enhancing medications in urban gay and bisexual men. *Sex Trans Infect* 2008; 84: 458–562.
21. Semple SJ, Zians J, Strathdee SA, et al. Sexual marathons and methamphetamine use among HIV-positive men who have sex with men. *Arch Sex Behav* 2009; 38: 583–590.
22. Sungkanuparph S, Techasathit W, Utaipiboon C, et al. Thai national guidelines for antiretroviral therapy in HIV-1 infected adults and adolescents. *Asian Biomed* 2010; 4: 515–528.